

# FD&C Yellow No. 6: Condensation of the Carcinogenesis Bioassay Technical Report\*

FD&C Yellow No. 6 (Sunset Yellow FCF, CAS No. 2783-94-0), a water-soluble monoazo dye, has been used since 1929 to impart a reddish-yellow color to various gelatin desserts, sherbets, carbonated beverages, candies, cereals, jams, pickles, smoked fish, puddings, medicinals (liquids, tablets, and capsules), toothpastes, hair rinses, and other foods, drugs, and cosmetics.

The Carcinogenesis Testing Program, National Cancer Institute (now part of the National Institute of Environmental Health Sciences/National Toxicology Program) selected and initiated a carcinogenesis bioassay on FD&C Yellow No. 6 because this chemical has wide use as a food colorant and in myriad other consumer products, indicating low level yet repeated exposure to a sizable population. Further, results available from other studies were considered inadequate for conclusive evaluation due to the small numbers of animals, low dose levels, and short exposure periods (1-4).

## Methods

Male and female inbred Fischer 344 rats and male and female hybrid B6C3F<sub>1</sub> mice, obtained from the Frederick Cancer Research Center, were used in this study. Control and treatment groups contained 50 animals of each sex and species, except for the control groups for rats, which consisted of 90 males and 90 females. For 103 consecutive weeks all groups received Ralston Purina Laboratory Chow meals. Treated groups were fed this diet containing

1.25% (12,500 ppm) or 2.5% (25,000 ppm) FD&C Yellow No. 6 (92% pure).

This carcinogenesis bioassay was conducted during December 1976-January 1979 at the Battelle Columbus Laboratories under a subcontract to Tracor Jitco (prime contractor for the program).

All animals that died during the study or that were killed at the end of the exposure period were subjected to a gross necropsy and a complete histopathological examination. Statistical analyses comparing survival and numbers of animals with specific site tumors were done with trend tests and pairwise comparisons (5-8). The study design conformed to the NCI Guidelines for carcinogen bioassay (9).

## Results

Mean body weights of high dose female rats and all low dose groups were comparable to the controls. High dose male rats and high dose male and female mice weighed somewhat less (10% or less) than the controls. Survival was comparable among all groups.

The incidences of FD&C Yellow No. 6-treated animals with specific site tumors did not differ significantly from those observed in controls. Tables 1 (rats) and 2 (mice) list those primary tumors occurring in at least three animals of any one group.

## Discussion

Hepatocellular carcinomas occurred in low dose (12,500 ppm) male mice at an incidence significantly higher than that in the controls (13/50, 26%; 22/48, 46%;  $p < 0.05$ ; 16/50, 32%); departure from linear trend was likewise evident ( $p < 0.05$ ), due mainly to a higher incidence in the low dose group. The historical control incidence (868/3,543, 24%) is sim-

\*Prepared by James Huff. National Toxicology Program, National Institute of Environmental Health Sciences, P. O. Box 12233, Research Triangle Park, North Carolina 27709.

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Table 1. Primary tumors in male and female F344 rats fed diets containing FD&amp;C Yellow No. 6.

Tumor	Males			Females		
	Control	12,500 ppm	25,000 ppm	Control	12,500 ppm	25,000 ppm
Adrenal cortical adenoma	3/89	2/50	0/49	6/86	2/50	4/50
Adrenal pheochromocytoma	14/89	3/50	11/49	4/86	1/50	4/50
Hepatocellular neoplastic nodule	5/90	6/50	1/50	3/88	3/50	0/50
Leukemia	22/90	12/50	17/50	16/88	12/50	10/50
Mammary gland	2/90	1/50	4/50	22/88	9/50	10/50
Pancreatic islet-cell adenoma or carcinoma	3/88	4/49	2/49	1/83	1/50	0/50
Pituitary chromophobe adenoma or carcinoma	5/84	5/46	4/46	30/83	18/45	17/48
Scutaneous fibroma or fibrosarcoma	5/90	2/50	3/50	2/88	0/50	0/50
Testicular interstitial cell	86/90	48/50	50/50	—	—	—
Thyroid C-cell carcinoma	2/89	4/49	4/50	3/86	2/50	2/48
Uterine endometrial stromal polyp	—	—	—	9/87	6/49	7/49

Table 2. Primary tumors in male and female B6C3F<sub>1</sub> mice fed diets containing FD&C Yellow No. 6.

Tumor	Males			Females		
	Control	12,500 ppm	25,000 ppm	Control	12,500 ppm	25,000 ppm
Lymphoma	9/50	1/49	10/50	15/50	5/50	10/49
Lung alveolar/bronchiolar adenoma or carcinoma	6/50	4/48	3/50	0/50	1/50	1/48
Hepatocellular adenoma	1/50	1/48	0/50	1/48	3/50	0/48
Hepatocellular carcinoma	13/50	22/48	16/50	7/48	0/50	4/48
Pituitary chromophobe adenoma or carcinoma	0/43	0/40	0/37	0/46	4/43	1/35
Skin and subcutaneous fibroma or sarcoma	5/50	5/49	6/50	0/50	0/50	0/49

ilar to the control rate in this study. Because the incidence of hepatocellular carcinomas in the 25,000 ppm group was not statistically different from controls and because the liver tumor occurrence in male B6C3F<sub>1</sub> mice is variable, the increased number of males with liver carcinoma cannot be clearly related to administration of FD&C Yellow No. 6.

Similarly, no other neoplastic or nonneoplastic lesions were considered induced by or associated with the administration of FD&C Yellow No. 6. Therefore, under the conditions of this bioassay, there was no clear evidence of carcinogenicity of FD&C Yellow No. 6 in F344 rats or B6C3F<sub>1</sub> mice of either sex (10).

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